Amendments to the Claims

Amendments to the claims are made in the Listing of Claims beginning on page 3 of this paper.

Remarks

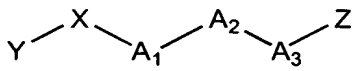
Remarks begin on page 16 of this paper.

Listing of Claims

Claims 1-26 (Canceled)

27. (New) A method of inhibiting platelet aggregation in a subject in need thereof comprising the steps of:

a) selecting a thrombin receptor antagonist compound of Formula I:



(I)

wherein

A_1 is an amino acid residue selected from the group consisting of cyclohexylalanine, Leu, Ile, Arg, Lys, Phe, substituted Phe, Tyr, and Trp;

A_2 is an amino acid residue selected from the group consisting of Lys, Orn, Arg, and homo Arg;

A_3 is an amino acid residue selected from the group consisting of Phe, substituted Phe, homo Phe, Tyr, Trp, phenylglycine, 2-thienylalanine, 3-thienylalanine, cyclohexylalanine, Leu, Ile, Asn, Gln, Arg, homo Arg, Orn, and Lys;

X is CO, CS, or SO_2;

Y is selected from the group consisting of aryl, substituted aryl, heterocycloalkyl, substituted heterocycloalkyl, heteroaryl, substituted heteroaryl, heteroarylethylenyl, substituted heteroarylethylenyl, arylacrylamidoheteroaryl, substituted arylacrylamidoheteroaryl, heteroarylacrylamidoheteroaryl, and substituted heteroarylacrylamidoheteroaryl, provided that Y is not pyrrolidinyl, phenyl, or 2-aminophenyl;

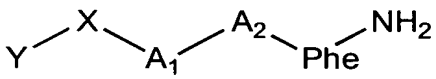
Z is NH_2, NH-alkyl, NH-aralkyl, or Arg-NH_2; and

wherein all amino acids are of the L configuration;

and any pharmaceutically acceptable salt thereof; and

b) administering to the subject a therapeutically effective amount of said compound.

28. (New) A method of Claim 27 wherein said compound is selected from a compound of Formula II:



(II)

wherein:

Y	A_1	A_2	X
5-(*o*-Cl-cinnamamido)triazol-3-yl	Cha	Arg	CO
5-(Thien-2-ylacrylamido) triazol-3-yl	Cha	Arg	CO
5-(Cinnamamido)triazol-3-yl	Cha	Arg	CO
5-(α–Me-cinnamamido) triazol-3-yl	Cha	Arg	CO
5-(α–Ph-cinnamamido) triazol-3-yl	Cha	Arg	CO
6-Cinnamamidopyridin-3-yl	Cha	Arg	CO
5-Cl, 3-Me-benzothiophen-2-yl	Cha	Arg	SO_2

Y	A_1	A_2	X
5-(p-F-cinnamamido) triazol-3-yl	Cha	Arg	CO
Benzothiophen-2-yl	Cha	Arg	CO
1-naphthyl	Cha	Arg	SO_2
2-naphthyl	Cha	Arg	SO_2 .

29. (New) A method of Claim 27 wherein said compound is selected from the group consisting essentially of:

[5-cinnamamidotriazol-3-yl]carbonyl-cyclohexylalanyl-arginyl-phenylalanineamide;

(6-Cinnamamidopyridin-3-yl)carbonyl-cyclohexylalanyl-arginyl-phenylalanineamide; and

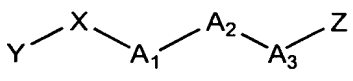
(5-Chloro-3-methyl-benzothiophen-2-yl)carbonyl-cyclohexylalanyl-arginyl-phenylalanineamide.

30. (New) The method of Claim 27, wherein the therapeutically effective amount of the compound is about 0.1 to about 300 mg/kg/day.

31. (New) The method of Claim 30, wherein the therapeutically effective amount of the compound is about 1 to about 50 mg/kg/day.

32. (New) A method of inducing platelet aggregation in a subject in need thereof comprising the steps of:

a) selecting a thrombin receptor agonist compound of Formula I:



(I)

wherein

A_1 is an amino acid residue selected from the group consisting of cyclohexylalanine, Leu, Ile, Arg, Lys, Phe, substituted Phe, Tyr, and Trp;

A_2 is an amino acid residue selected from the group consisting of Lys, Orn, Arg, and homo Arg;

A_3 is an amino acid residue selected from the group consisting of Phe, substituted Phe, homo Phe, Tyr, Trp, phenylglycine, 2-thienylalanine, 3-thienylalanine, cyclohexylalanine, Leu, Ile, Asn, Gln, Arg, homo Arg, Orn, and Lys;

X is CO, CS, or SO_2;

Y is selected from the group consisting of aryl, substituted aryl, heterocycloalkyl, substituted heterocycloalkyl, heteroaryl, substituted heteroaryl, heteroarylethylenyl, substituted heteroarylethylenyl, arylacrylamidoheteroaryl, substituted arylacrylamidoheteroaryl, heteroarylacrylamidoheteroaryl, and substituted heteroarylacrylamidoheteroaryl, provided that Y is not pyrrolidinyl, phenyl, or 2-aminophenyl;

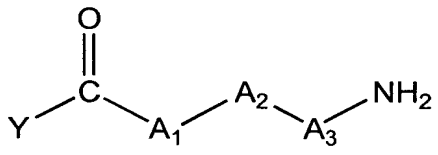
Z is NH_2, NH-alkyl, NH-aralkyl, or Arg-NH_2; and

wherein all amino acids are of the L configuration;

and any pharmaceutically acceptable salt thereof; and

b) administering to the subject a therapeutically effective amount of said compound.

33. (New) A method of Claim 32 wherein said compound is selected from a compound of Formula III:



(III)

wherein:

Y	A_1	A_2	A_3
5-H_2N-1,2,4-triazol-3-yl	Cha	Arg	Phe
5-Bromopyridin-3-yl	Cha	Arg	Phe
2-Chromonyl	Cha	Arg	Phe
5-(α–Me-cinnamamido)triazol-3-yl	Cha	Arg	Phe
5-Naphthylacrylamidotriazol-3-yl	Cha	Arg	Phe
Quinoxalin-2-yl	Cha	Arg	Phe
5-(*o*–Cl-cinnamamido)triazol-3-yl	Cha	Arg	Phe
6-Aminopyridin-3-yl	Cha	Arg	Phe
5-H_2N-1,2,4-triazol-3-yl	Cha	Arg	Phe-Arg
Thiadiazol-4-yl	Cha	Arg	Phe
5-(2,3-diMeO-cinnamamido)triazol-3-yl	Cha	Arg	Phe
5-(α–F-cinnamamido)triazol-3-yl	Cha	Arg	Phe
5-(*m*-NO_2-cinnamamido)triazol-3-yl	Cha	Arg	Phe
5-(*o*-NO_2-cinnamamido)triazol-3-yl	Cha	Arg	Phe
Pyridin-3-yl	Cha	Arg	Phe

Y	A_1	A_2	A_3
5-(*m*-Cl-cinnamamido)triazol-3-yl	Cha	Arg	Phe
5-H_2N-1,2,4-triazol-3-yl	Phe	Arg	Phe
5-H_2N-1,2,4-triazol-3-yl	Cha	Lys	Phe
5-H_2N-1,2,4-triazol-3-yl	Cha	Arg	Cha
5-H_2N-1,2,4-triazol-3-yl	Cha	Arg	Phgly
5-(thiophen-2-ylacrylamido)triazol-3-yl	Cha	Arg	Phe
3-H_2N-pyrazin-2-yl	Cha	Arg	Phe
trans 2-(3-pyridyl)ethylenyl	Cha	Arg	Phe
5-(*p*-MeO-cinnamamido)triazol-3-yl	Cha	Arg	Phe
5-(*p*-CN-cinnamamido)triazol-3-yl	Cha	Arg	Phe
5-(*p*-F-cinnamamido)triazol-3-yl	Cha	Arg	Phe
2-H_2N-pyridin-3-yl	Cha	Arg	Phe
5-H_2N-1,2,4-triazol-3-yl	Cha	Arg	Tyr
5-H_2N-1,2,4-triazol-3-yl	Cha	Arg	2-Thala
Pyridin-2-yl	Cha	Arg	Phe
5-(*p*-Phenyl-cinnamamido)triazol-3-yl	Cha	Arg	Phe

Y	A_1	A_2	A_3
N-(*p*-F-phenylalanyl)-piperidin-3-yl	Cha	Arg	Phe
5-(Cinnamamido)triazol-3-yl	Cha	Arg	Phe
5-(α–phenyl-cinnamamido)triazol-3-yl	Cha	Arg	Phe
3-aminophenyl	Cha	Arg	Phe
1-biphenyl	Cha	Arg	Phe
2-biphenylenyl	Cha	Arg	Phe
benzimidazol-5-yl	Cha	Arg	Phe .

34. (New) A method of Claim 32 wherein said compound is selected from the group consisting essentially of:

(5-Bromopyridin-3-yl)carbonyl-cyclohexylalanyl-arginyl-phenylalanineamide;

2-Chromonylcarbonyl-cyclohexylalanyl-arginyl-phenylalanineamide;

(5-Aminotriazol-3-yl)carbonyl-cyclohexylalanyl-arginyl-phenylalanineamide;

[5-(α-Methyl)cinnamamidotriazol-3-yl]carbonyl-cyclohexylalanyl-arginyl-phenylalanineamide;

{5-[3-(1-Naphthyl)acrylamido]triazol-3-yl}carbonyl-cyclohexylalanyl-arginyl-phenylalanineamide;

[Quinoxalin-2-yl]carbonyl-cyclohexylalanyl-arginyl-phenylalanineamide;

[5-(*o*-Chlorocinnamamido)triazol-3-yl]carbonyl-cyclohexylalanyl-arginyl-phenylalanineamide;

(6-Aminopyridin-3-yl)carbonyl-cyclohexylalanyl-arginyl-phenylalanineamide;

(5-Aminotriazol-3-yl)carbonyl-phenylalanyl-arginyl-phenylalanyl-arginineamide;

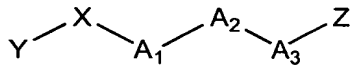
(5-Aminotriazol-3-yl)carbonyl-cyclohexylalanyl-lysinyl-phenylalanineamide; and

{5-[3-(2-Thienyl)acrylamido]triazol-3-yl}carbonyl-cyclohexylalanyl-arginyl-phenylalanineamide.

35. (New) The method of Claim 32, wherein the therapeutically effective amount of the compound is about 0.1 to about 300 mg/kg/day.

36. (New) The method of Claim 35, wherein the therapeutically effective amount of the compound is about 1 to about 50 mg/kg/day.

37. (New) A method of treating a platelet-mediated thrombotic disorder selected from the group consisting of myocardial infarction, stroke, angina, and ischemic attacks in a subject in need thereof comprising administering to the subject a therapeutically effective amount of a compound of Formula I:



(I)

wherein

A_1 is an amino acid residue selected from the group consisting of cyclohexylalanine, Leu, Ile, Arg, Lys, Phe, substituted Phe, Tyr, and Trp;

A_2 is an amino acid residue selected from the group consisting of Lys, Orn, Arg, and homo Arg;

A_3 is an amino acid residue selected from the group consisting of Phe, substituted Phe, homo Phe, Tyr, Trp, phenylglycine, 2-thienylalanine, 3-thienylalanine, cyclohexylalanine, Leu, Ile, Asn, Gln, Arg, homo Arg, Orn, and Lys;

X is CO, CS, or SO_2;

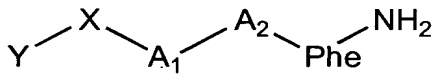
Y is selected from the group consisting of aryl, substituted aryl, heterocycloalkyl, substituted heterocycloalkyl, heteroaryl, substituted heteroaryl, heteroarylethylenyl, substituted heteroarylethylenyl, arylacrylamidoheteroaryl, substituted arylacrylamidoheteroaryl, heteroarylacrylamidoheteroaryl, and substituted heteroarylacrylamidoheteroaryl, provided that Y is not pyrrolidinyl, phenyl, or 2-aminophenyl;

Z is NH_2, NH-alkyl, NH-aralkyl, or Arg-NH_2; and

wherein all amino acids are of the L configuration;

and any pharmaceutically acceptable salt thereof.

38. (New) A method of Claim 37 wherein said compound is selected from a compound of Formula II:



(II)

wherein:

Y	A_1	A_2	X
5-(*o*-Cl-cinnamamido)triazol-3-yl	Cha	Arg	CO
5-(Thien-2-ylacrylamido) triazol-3-yl	Cha	Arg	CO
5-(Cinnamamido)triazol-3-yl	Cha	Arg	CO
5-(α–Me-cinnamamido) triazol-3-yl	Cha	Arg	CO

Y	A_1	A_2	X
5-(α–Ph-cinnamamido) triazol-3-yl	Cha	Arg	CO
6-Cinnamamidopyridin-3-yl	Cha	Arg	CO
5-Cl, 3-Me-benzothiophen-2-yl	Cha	Arg	SO_2
5-(p-F-cinnamamido) triazol-3-yl	Cha	Arg	CO
Benzothiophen-2-yl	Cha	Arg	CO
1-naphthyl	Cha	Arg	SO_2
2-naphthyl	Cha	Arg	SO_2 .

39. (New) A method of Claim 37 wherein said compound is selected from the group consisting essentially of:

[5-cinnamamidotriazol-3-yl]carbonyl-cyclohexylalanyl-arginyl-phenylalanineamide;

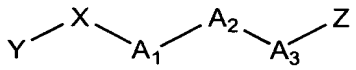
(6-Cinnamamidopyridin-3-yl)carbonyl-cyclohexylalanyl-arginyl-phenylalanineamide; and

(5-Chloro-3-methyl-benzothiophen-2-yl)carbonyl-cyclohexylalanyl-arginyl-phenylalanineamide.

40. (New) The method of Claim 37, wherein the therapeutically effective amount of the compound is about 0.1 to about 300 mg/kg/day.

41. (New) The method of Claim 40, wherein the therapeutically effective amount of the compound is about 1 to about 50 mg/kg/day.

42. (New) A method of treating restenosis in a subject in need thereof comprising administering to the subject a therapeutically effective amount of a compound of Formula I:



(I)

wherein

A_1 is an amino acid residue selected from the group consisting of cyclohexylalanine, Leu, Ile, Arg, Lys, Phe, substituted Phe, Tyr, and Trp;

A_2 is an amino acid residue selected from the group consisting of Lys, Orn, Arg, and homo Arg;

A_3 is an amino acid residue selected from the group consisting of Phe, substituted Phe, homo Phe, Tyr, Trp, phenylglycine, 2-thienylalanine, 3-thienylalanine, cyclohexylalanine, Leu, Ile, Asn, Gln, Arg, homo Arg, Orn, and Lys;

X is CO, CS, or SO_2;

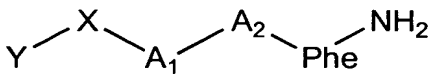
Y is selected from the group consisting of aryl, substituted aryl, heterocycloalkyl, substituted heterocycloalkyl, heteroaryl, substituted heteroaryl, heteroarylethylenyl, substituted heteroarylethylenyl, arylacrylamidoheteroaryl, substituted arylacrylamidoheteroaryl, heteroarylacrylamidoheteroaryl, and substituted heteroarylacrylamidoheteroaryl, provided that Y is not pyrrolidinyl, phenyl, or 2-aminophenyl;

Z is NH_2, NH-alkyl, NH-aralkyl, or Arg-NH_2; and

wherein all amino acids are of the L configuration;

and any pharmaceutically acceptable salt thereof.

43. (New) A method of Claim 42 wherein said compound is selected from a compound of Formula II:



(II)

wherein:

Y	A_1	A_2	X
5-(*o*-Cl-cinnamamido)triazol-3-yl	Cha	Arg	CO
5-(Thien-2-ylacrylamido) triazol-3-yl	Cha	Arg	CO
5-(Cinnamamido)triazol-3-yl	Cha	Arg	CO
5-(α–Me-cinnamamido) triazol-3-yl	Cha	Arg	CO
5-(α–Ph-cinnamamido) triazol-3-yl	Cha	Arg	CO
6-Cinnamamidopyridin-3-yl	Cha	Arg	CO
5-Cl, 3-Me-benzothiophen-2-yl	Cha	Arg	SO_2
5-(p-F-cinnamamido) triazol-3-yl	Cha	Arg	CO
Benzothiophen-2-yl	Cha	Arg	CO
1-naphthyl	Cha	Arg	SO_2

Y	A_1	A_2	X
2-naphthyl	Cha	Arg	SO_2 .

44. (New) A method of Claim 42 wherein said compound is selected from the group consisting essentially of:

[5-cinnamamidotriazol-3-yl]carbonyl-cyclohexylalanyl-arginyl-phenylalanineamide;

(6-Cinnamamidopyridin-3-yl)carbonyl-cyclohexylalanyl-arginyl-phenylalanineamide; and

(5-Chloro-3-methyl-benzothiophen-2-yl)carbonyl-cyclohexylalanyl-arginyl-phenylalanineamide.

45. (New) The method of Claim 42, wherein the therapeutically effective amount of the compound is about 0.1 to about 300 mg/kg/day.

46. (New) The method of Claim 45, wherein the therapeutically effective amount of the compound is about 1 to about 50 mg/kg/day.